sequence of SEQ ID NO: 1, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, or SEQ ID NO: 47, or degenerate variants thereof, and wherein said nucleic acid encodes the amino acid sequence of SEQ ID NO: 2, SEQ ID NO: 42, SEQ ID NO: 44, SEQ ID NO: 46, or SEQ ID NO: 48, respectively.

C1 Cont

36. (Amended) A substantially pure nucleic acid having a polynucleotide sequence that has at least 50% sequence identity to SEQ ID NO: 1 over the entire length of SEQ ID NO: 1.

C2

37. (Amended) The nucleic acid of claim 36, having a polynucleotide sequence that has at least 85% sequence identity to SEQ ID NO: 1 over the entire length of SEQ ID NO: 1.

38. (Amended) The nucleic acid of claim 37, having a polynucleotide sequence that has at least 95% sequence identity to SEQ ID NO: 1 over the entire length of SEQ ID NO: 1.

41. (Amended) A substantially pure nucleic acid having a polynucleotide sequence that has at least 50% sequence identity to the corresponding region of SEQ ID NO: 1, wherein said nucleic acid comprises a naturally-occurring mammalian methionine synthase reductase mutation or polymorphism.

C3

42. (Amended) The nucleic acid of claim 41, having a polynucleotide sequence that has at least 85% sequence identity to the corresponding region of SEQ ID NO: 1.

43. (Amended) The nucleic acid of claim 42, having a polynucleotide sequence that has at least 95% sequence identity to the corresponding region of SEQ ID NO: 1.

Add the following new claims 48-53.

48. (New) The nucleic acid of claim 47, wherein said binding site comprises a sequence that is at least 70% identical to one of the following sequences:

(a) FLLLYATQQGQAKAIAEEMC (SEQ ID NO: 52),

(b) VVVVSTTGTGDPPDTARKFVKEI (SEQ ID NO: 53),

(c) AHLRYGLLGLGDSEYTYFCNGGKIIDKRL (SEQ ID NO: 54),

(d) LQPRPYSCASSSLFHPGKL (SEQ ID NO: 55),

(e) FVFNIVEFLSTATT (SEQ ID NO: 56),

(f) LRKGVCTGWLALLVASV (SEQ ID NO: 57),

(g) IPIIMVGPGTGIAPFIGFLQHR (SEQ ID NO: 58),

(h) SFSRDA (SEQ ID NO: 59),

(i) APAKYVQDNIQLHGQQVARILLQENGHIYVCGDAKNMAKDV (SEQ ID NO: 60), or

(j) KRYLQDIWS (SEQ ID NO: 61).

49. (New) The nucleic acid of claim 48, wherein said binding site comprises a sequence that is identical to one of the following sequences:

(a) FLLLYATQQGQAKAIAEEMC (SEQ ID NO: 52),

(b) VVVVSTTGTGDPPDTARKFVKEI (SEQ ID NO: 53),

(c) AHLRYGLLGLGDSEYTYFCNGGKIIDKRL (SEQ ID NO: 54),

(d) LQPRPYSCASSSLFHPGKL (SEQ ID NO: 55),

(e) FVFNIVEFLSTATT (SEQ ID NO: 56),

(f) LRKGVCTGWLALLVASV (SEQ ID NO: 57),

(g) IPIIMVGPGTGIAPFIGFLQHR (SEQ ID NO: 58),

(h) SFSRDA (SEQ ID NO: 59),

(i) APAKYVQDNIQLHGQQVARILLQENGHIYVCGDAKNMAKDV (SEQ ID NO: 60), or

(j) KRYLQDIWS (SEQ ID NO: 61).

50. (New) The nucleic acid of claim 47, wherein said binding site comprises any one of SEQ ID NOs: 25-40.

51. (New) The nucleic acid of claim 4 or 41, wherein the administration of said nucleic acid to a subject leads to a decrease in the activity of a mutant or polymorphic methionine synthase reductase polypeptide in said subject.

52. (New) The nucleic acid of claim 51, wherein the administration of said nucleic leads to a decrease in the activity of said mutant methionine synthase reductase polypeptide.

53. (New) The nucleic acid of claim 4 or 41, wherein said nucleic acid comprises said naturally-occurring mammalian methionine synthase reductase mutation.

In the Specification

Kindly replace the Sequence Listing with the enclosed amended Sequence Listing.

REMARKS

The invention features the cloning of mammalian methionine synthase reductase. Accordingly, the invention provides wild-type and mutant mammalian methionine synthase reductase nucleic acids.

Examination of claims 1-5 and 35-47 is reported in the present Office Action. Claims 36-38 and 41-43 were objected to because of improper sequence identifiers. Claims 3 and 47 were rejected under 35 U.S.C. § 112, second paragraph, and claims 1, 2, 4, 5, and 35-47 were rejected under 35 U.S.C. § 112, first paragraph. Each of the rejections is addressed below in the order that they appear in the Office Action.